concomitantly on both arms 1p and 13q, 1p and 8p as well as 6q and 13q was significantly higher in tumors arising from CH than LC (the number of HCCs with CH vs. LC showing LOH in above combinations were 16 vs. 5, 16 vs. 6, and 14 vs. 3 respectively).

IN THE CLAIMS:

Please cancel claims 2-17 and 21-27.

Please amend claim 18 as follows:

18. (Amended) A tumor suppressor gene polynucleotide involved in the occurrence of a HCC in a patient obtained by a process comprising:

a) constructing a cosmid library from a selected YAC clone;

b) selecting cosmid clones of interest by colony hybridization with labeled human genomic DNA as a probe;

c) constructing a contig map of the purified selected cosmid clones;

d) performing an exon amplification reaction and inserting the reverse transcribed RNA fragments in a suitable vector;

e) hybridizing the inserts of step d) with a suitable human cDNA library, preferably a fetal or adult liver cDNA library and selecting the hybridizable cDNA clones; and

f) sequencing the selected cDNA clones inserts and characterizing the coding sequences.

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Please add the following new claims:

28. (New) A tumor suppressor gene associated with hepatocellular carcinoma in a patient obtained by a process comprising:

a) constructing a cosmid library from a YAC clone containing a genomic DNA of interest;

b) selecting cosmid clones of interest by colony hybridization with labeled human genomic DNA as a probe;

c) performing an exon amplification reaction using DNA from the selected cosmid clones and resulting in reverse transcribed sequences;

d) hybridizing the reverse transcribed sequences with a human cDNA library;

e) selecting hybridized cDNA clones;

f) sequencing the selected cDNA clones; and

g) characterizing the coding sequences of the tumor suppressor gene.

29. (New) An oligonucleotide fragment of the tumor suppressor gene of claim 28 obtained by restriction enzyme cleavage or chemical synthesis.

30. (New) A method for producing a polypeptide encoded by a tumor suppressor gene associated with hepatocellular carcinoma, said method comprising:

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a) optionally amplifying a nucleic acid of the tumor suppressor gene that encodes the desired polypeptide using a pair of oligonucleotide fragments according to claim 29;

b) inserting the nucleic acid in a recombinant vector;

c) transforming or transfecting a cell host with the recombinant vector;

d) culturing, in an appropriate culture medium, the transformed or transfected cell host; and

e) separating or purifying the polypeptide of interest from said culture medium, or from a host cell lysate.

31. (New) A method for discriminating between a diagnosis of hepatocellular carcinoma with liver cirrhosis and a diagnosis of hepatocellular carcinoma with chronic hepatitis lesions, comprising:

a) providing genomic DNA from a first tissue sample from an organ other than the liver of said patient and from a second tissue sample from the liver of said patient;

b) amplifying the genomic DNA of step a) with a first pair of primers and a second pair of primers, wherein the first pair of primers amplifies a first polymorphic microsatellite DNA marker and the second pair of primers amplifies a second polymorphic microsatellite DNA marker, wherein:

1) the first polymorphic microsatellite DNA marker is located within the chromosomal

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region 1p and is D1S199; and the second polymorphic microsatellite DNA marker is located within the chromosomal region 13q and is selected from the group consisting of D13S171 and D13S284; or

2) the first polymorphic microsatellite DNA marker is located within the chromosomal region 1p and is D1S199; and the second polymorphic microsatellite DNA marker is located within the chromosomal region 8p and is selected from the group consisting of D8S264, D8S262, D8S518, D8S1742, D8S1819, D8S1721, D8S1731, and D8S1752; or

3) the first polymorphic microsatellite DNA marker is located within the chromosomal region 6q and is selected from the group consisting of D6S290 and D6S305; and the second polymorphic microsatellite DNA marker is located within the chromosomal region 13q and is selected from the group consisting of D13S171 and D13S284;

c) detecting a genetic alteration by comparing amplified DNA of step b) derived, respectively, from the first and the second tissue sample,

wherein a higher frequency of concomitant detection of the genetic alteration correlates with the diagnosis of hepatocellular carcinoma with chronic hepatitis lesions rather

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than the diagnosis of hepatocellular carcinoma with liver cirrhosis.

32. (New) A method for diagnosing invasive hepatocellular carcinoma, comprising:

a) providing genomic DNA from a first tissue sample from an organ other than the liver of a patient and from a second tissue sample from the liver of said patient;

b) amplifying the genomic DNA of step a) with a first pair of primers and a second pair of primers, wherein the first pair of primers amplifies a first polymorphic microsatellite DNA marker and the second pair of primers amplifies a second polymorphic microsatellite DNA marker, wherein the first polymorphic microsatellite DNA marker is located within the chromosomal region 16p and is D16S420; and the second polymorphic microsatellite DNA marker is located within the chromosomal region 17p and is selected from the group consisting of D17S787 and D17S928; and

c) detecting a genetic alteration by comparing amplified DNA of step b) derived, respectively, from the first and the second tissue sample, wherein detection of the genetic alteration is correlated with the diagnosis of invasive hepatocellular carcinoma.

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33. (New) A method for detecting a genetic abnormality linked to hepatocellular carcinoma in a biological sample containing DNA or cDNA, comprising:

a) contacting the DNA or cDNA in the biological sample with at least one pair of primers, wherein the at least one pair of primers amplifies a polymorphic microsatellite DNA marker located within a chromosomal region selected from the group consisting of 1q, 7q, 8q, 9p, 14q, and 17q;

b) amplifying the DNA or cDNA; and

c) detecting the genetic abnormality in an amplified DNA or cDNA of step b), wherein the genetic abnormality is linked to hepatocellular carcinoma.

34. (New) A diagnostic kit for detecting a genetic abnormality linked to hepatocellular carcinoma, comprising:

a) at least one pair of primers, wherein the at least one pair of primers amplifies a polymorphic microsatellite DNA marker located within a chromosomal region selected from the group consisting of 1q, 7q, 8q, 9p, 14q, 17q, 1p, 4q, 7p, 8p, 10q, 13q, 16p, 16q, and 17p;

b) reagents necessary for carrying out a DNA amplification; and

c) a component for determining a length of an amplified DNA or for detecting a mutation.

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